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Influence of Operational Variables on Ball-Milling of Sulfadimethoxine and White Alundum

NOBUYOSHI KANENIWA, AKIKO IKEKAWA, and KATSUYO HASHIMOTO

School of Pharmaceutical Sciences, Showa University[1]

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In the previous paper, thirty two kinds of organic and inorganic powders were ball-milled and the rate of an increase of surface area by ball-milling was considered to depend on coherency of powder particles expressed as a function of surface energy, melting point, solubility in water, true density and so on.[2] In this paper, influence of operational variables on the rate of an increase of surface area of sulfadimethoxine and white alundum by ball-milling was investigated.

Experimental

The materials used were sulfadimethoxine offered from Chugai Seiyaku Kogyo Co. and white alundum (Type 500) purchased from Nishio Kogyo Co.

Various amounts of ceramic balls with true density of 2.4 g/cm^3 and in diameter between 1.4 cm and 3.5 cm were inserted in a ceramic mill in the inside diameter between 8 cm and 14 cm and in capacity between 450 ml and 3430 ml. Various amounts of stainless steel balls with true density of 8.2 g/cm^3 and in diameter of 1.9 cm and 2.5 cm were inserted in a stainless steel mill in the inside diameter of 10 cm and in capacity of 870 ml. Various maounts of materials were ball-milled in these mills with the revolving velocity of a mill between 90 rpm and 210 rpm. Surface area of ball-milled samples was measured by air permeability method.[3]

Result and Discussion

The rate of an increase of surface area decreased gradually with the lapse of ball-milling time. (Fig. 1) As shown in Fig. 2, equation (1) applied well, where S was specific surface area of a sample, and k_1 and k_2 were parameters dependent on physicochemical properties of ball-milled samples, operational variables and so on.[2]

$$dS/dt = k_1 \exp(-k_2 S) \quad (1)$$

Parameter k_1 is identical with dS/dt for the sample whose surface area is negligibly small. In the previous paper, k_2 was small for the sample with high melting point and little solubility in water.[2] Probably, k_2 is a parameter concerning a decrease of dS/dt due to coherency of particles caused by an increase of surface area by ball-milling.

1) Influence of a Revolving Velocity of a Mill on Parameters k_1 and k_2

The way how balls move in a revolving mill is considered to depend on the balance of the gravitational force of balls and the centrifugal force given to balls by the revolution of a mill. If N_c is the revolving velocity of a mill when the gravitational force of balls is equal to the centrifugal force, equation (2) is applied and N_c is represented by equation (3), where m_b is the weight of a ball, D is the inside diameter of a mill, d is a diameter of a ball and g is the gravitational constant.

1) *Hatanodai, 1-5-8, Shinagawa-ku, Tokyo.*
2) A. Ikekawa, K. Imagawa, T. Omori, N. Kaneniwa, *Chem. Pharm. Bull.* (Tokyo), **19**, 1027 (1971).
3) E. Suito, M. Arakawa, M. Takahashi, *Kogyo Kagaku Zasshi*, **59**, 307 (1956).

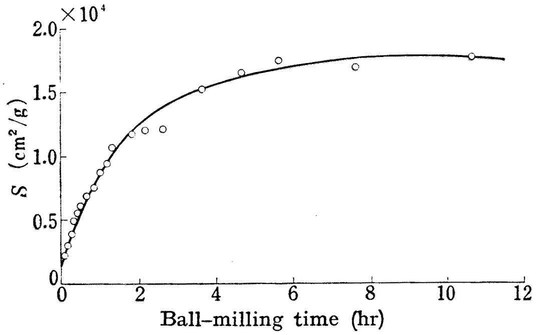

Fig. 1. Increase of Surface Area of Sulfadimethoxine with the Lapse of Ball-Milling Time

ceramic mill, $D=8$ cm, $N/N_c=0.76$, $W_s=20$ g, $J_b=0.25$
The ratio of the number of balls in diameter of 2.5 cm to that of balls in diameter of 1.9 cm was 1/3.

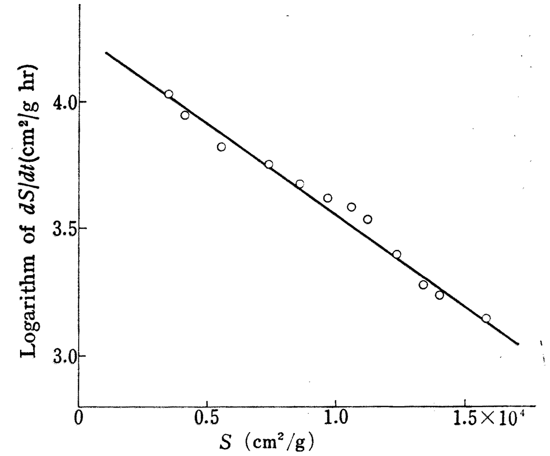

Fig. 2. Application of Equation (1) to Ball-Milling of Sulfadimethoxine

ceramic mill, $D=8$ cm, $N/N_c=0.76$, $W_s=20$ g, $J_b=0.25$
The ratio of the number of balls in diameter of 2.5 cm to that of balls in diameter of 1.9 cm was 1/3.

$$m_b g = (1/2)m_b(D-d)(2\pi N_c)^2 \quad (2)$$

$$N_c = (1/2\pi)\sqrt{2g/(D-d)} \quad (3).$$

A transparent acrylic lid was sticked on a mill with a vinyl tape and the movement of balls in a revolving mill was observed. When the revolving velocity of a mill, N, was smaller than N_c, balls rolled down over the layers of another balls successively after held up to a certain height by the wall of a revolving mill. Matsui, *et al.* reported that a decrease of particle size was mainly attributed to impact stress of balls rolling down over the layers of another balls when the apparent volume of balls in loosest packing was nearly half the volume of a mill, the apparent volume of a sample was approximately equal to the space between balls in loosest packing and N/N_c was 0.7.[4] When N/N_c was larger than 1.0, the balls rotating along the wall of a mill by a centrifugal force collided each another. In this case, a decrease of particle size is probably attributed to impact stress by collision between balls.

Porosity of balls, ε_b, was assumed to be 0.50 in consideration of a wall effect because of the large value of d/D, and the ratio of the apparent volume of balls in loosest packing to the inside volume of a mill, J_b, was calluculated by equation (4), where W_b was the total weight of balls, ρ_b was the true density of balls and V_m was the inside volume of a mill.

$$J_b = (W_b/\rho_b)/V_m(1-\varepsilon_b) \quad (4)$$

In case of 0.42 of J_b, k_1/N was the largest and k_2 was the smallest when N/N_c was around 0.70. When J_b was equal to or larger than 0.65, both k_1/N and k_2 decreased with an increase of N/N_c. (Fig. 3 and 4) When J_b was 0.65, the distance between the lid of a mill and the top of the layers of balls was approximately equal to the diameter of balls because of the large value of d/D, and it was a little difficult to obtain J_b larger than 0.65. Balls may move more smoothly as N/N_c decreased, in case of J_b equal to or larger than 0.65. In this case, a decrease of particle size is probably due to compression and shear between balls or between balls and the wall of a mill.

4) K. Matsui, T. Kurihara, T. Sekiguchi, *Kagaku Kogaku*, **34**, 881 (1970).

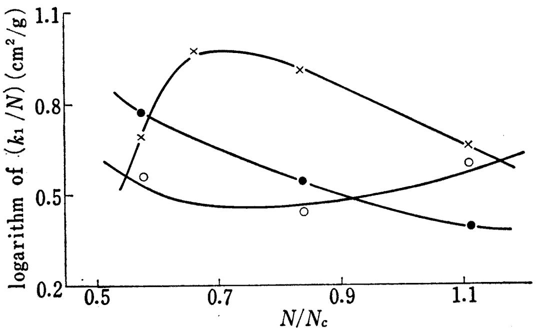

Fig. 3. Influence of the Revolving Velocity of a Mill on Parameter k_1 for Sulfadimethoxine

ceramic mill, $D=8$ cm, $W_s=30$ g,
The ratio of the number of balls in diameter of 2.5 cm to that of balls in diameter of 1.9 cm was 1/3.
J_b: ○: 017, ×: 0.42, ●: 0.65

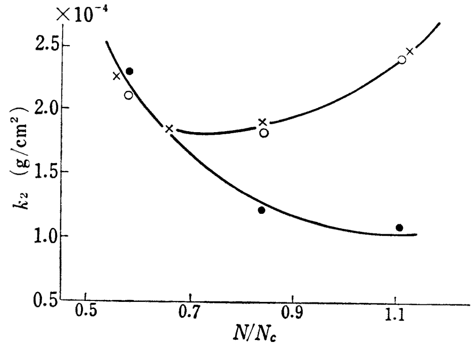

Fig. 4. Influence of the Revolving Velocity of a Mill on Parameter k_2 for Sulfadimethoxine

ceramic mill, $D=8$ cm, $W_s=30$ g
The ratio of the number of balls in diameter of 2.5 cm to that of the balls in diameter of 1.9 cm was 1/3.
J_b: ○: 0.17, ×: 0.42, ●: 0.65

2) Influence of J_b on Parameters k_1 and k_2

In case of N/N_c smaller than 1.0, k_1 increased in proportion to the α th power of J_b when J_b was smaller than 0.5, and α was 1.8 for sulfadimethoxine in case of 0.85 of N/N_c and α was 2.1 for sulfadimethoxine in case of 0.55 of N/N_c and for white alundum in case of 0.70 of N/N_c. When J_b was larger than 0.50, k_1 decreased with an increase of J_b. But k_1 increased again when J_b was equal to or larger than 0.65 and N/N_c was smaller than 0.85. (Fig. 5) In case of N/N_c larger than 1.0, k_1 was large and influenced little by J_b between 0.15 and 0.45. (Fig. 6) Parameter k_2 was influenced little by J_b.

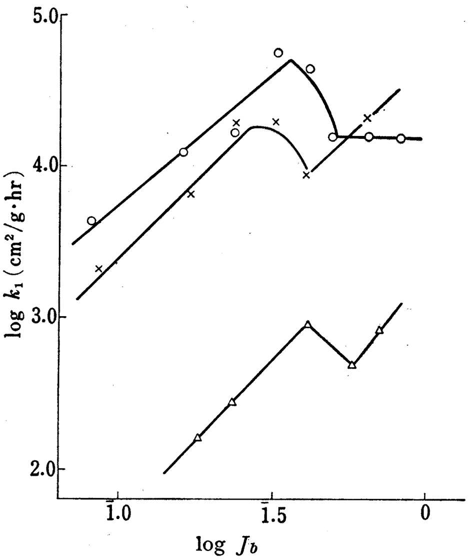

Fig. 5. Influence of J_b on Parameter k_1 for Sulfadimethoxine and White Alundum

ceramic mill, D=8 cm
sulfadimethoxine, $W_S=20$ g, $N/N_C=0.85$, ○
$W_S=30$ g, $N/N_C=0.55$ ×
The ratio of the number of balls in diameter of 2.5 cm to that of balls in diameter of 1.9 cm was 1/3.
white alundum, $W_S=25$ g, $N/N_C=0.70$, $d=2.5$ cm △

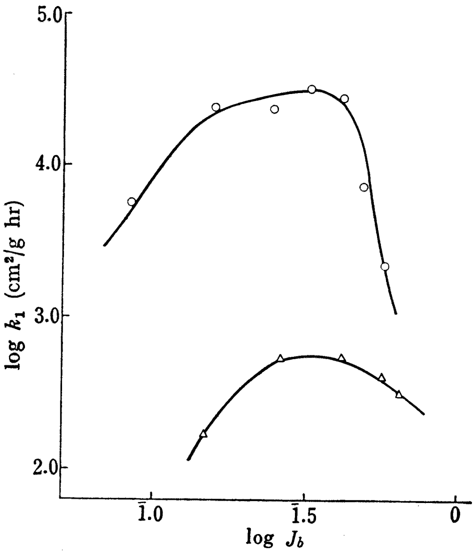

Fig. 6. Influence of J_b on Parameter k_1 for Sulfadimethoxine and White Alundum

ceramic mill, $D=8$ cm, $N/N_C=1.1$
○: :sulfadimethoxine, $W_S=20$ g
The ratio of the number of balls in diameter of 2.5 cm to that of balls in diameter of 1.9 cm was 1/3.
△: white alundum, $W_S=25$ g, $d=1.9$ cm

3) Influence of the Apparent Volume of the Inserted Sample on Parameters k_1 and k_2

Approximately, k_1 was inversely proportional to the 1.6 th power of the volume of the inserted sample in case of 0.85 of N/N_c in the previous paper.[2] But detailed investigation showed that k_1 for the case that the apparent volume of the sample was much larger than the space between balls in loosest packing was smaller than the value expected from the straight line obtained by the logarithmic plot of k_1 versus the volume of the sample equal to or smaller than the space between balls in loosest packing. The ratio of the apparent volume of the sample to the inside volume of a mill was represented by equation (5), where W_s was the total weight of the sample, ρ_s was the true density of the sample and ε_s was the porosity of the sample.

$$J_s = (W_s/\rho_s)/V_m(1-\varepsilon_s) \qquad (5)$$

In the previous paper, porosity of crushed white alundum with specific surface diameter between 1.0 μ and 10.0 μ in loosest packing was between 0.75 and 0.80, and that of the crushed sulfadimethoxine with specific diameter between 1.0 μ and 30.0 μ in loosest packing was between 0.70 and 0.75.[2] Then, the values of J_s were calcullated by equation (5), under the assumption that ε_b for white alundum was 0.75 and that for sulfadimethoxine was 0.70. The value of $J_s/\varepsilon_b J_b$ is identical with the ratio of the apparent volume of the sample to the space between balls in loosest packing. As shown in Fig. 7, straight lines were obtained by the logarithmic plot of k_1 versus $J_s/\varepsilon_b J_b$ smaller than 1.0, and k_1 in case of $J_s/\varepsilon_b J_b$ larger than 1.0 was under these lines. The tangent of these straight lines, $-\beta$, was small for sticky powders and in case of large N/N_c (Table I). Parameter k_2 was influenced little by the apparent volume of the sample inserted in a mill.

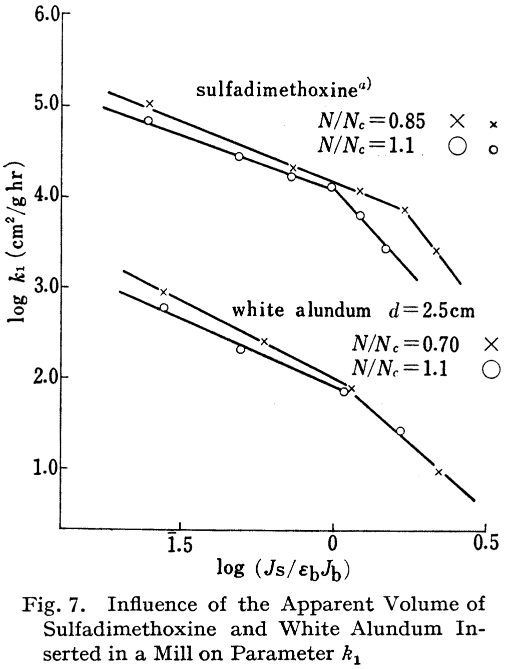

Fig. 7. Influence of the Apparent Volume of Sulfadimethoxine and White Alundum Inserted in a Mill on Parameter k_1

ceramic mill, D=8 cm, J_b=0.42

a) In case of sulfadimethoxine, the ratio of the number of balls in diameter of 2.5 cm to that of balls in diameter of 1.9 cm was 1/3.

Table I. The Value of β for Sulfadimethoxine and White Alundum

	Ceramic mill, D=8 cm, J_b=0.42		
	d	N/N_c	β
Sulfadimethoxine	a)	0.85	1.36
	a)	1.1	1.14
White alundum	2.5cm	0.70	1.72
	2.5cm	1.1	1.48

a) The ratio of the number of balls in diameter of 2.5 cm to that of balls in diameter of 1.9 cm was 1/3.

4) Influence of the Inside Diameter of a Mill and the Diameter of Balls on Parameters k_1 and k_2

As shown in Fig. 8 and 9, the inside diameter of a mill and the diameter of balls influenced little on parameters k_1 and k_2. The same results were also obtained by ball-milling eleven kinds of organic and inorganic powders other than sulfadimethoxine and white alundum. Fig. 9 shows the result for ball-milling by balls of an equal size. The value of k_1 for ball-milling by the mixture of large balls and small balls was identical with the value for ball-milling by balls of an equal size.

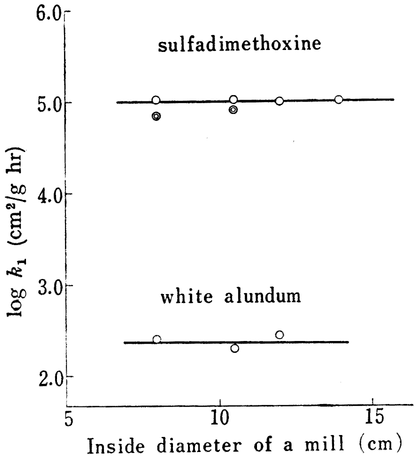

Fig. 8. Influence of the Inside Diameter of a Mill on Parameter k_1 for Sulfadimethoxine and White Alundum

ceramic mill, J_b=0.42
sulfadimethoxine, J_S=0.038
The ratio of the number of balls in diameter of 2.5 cm to that of balls in diameter of 1.9cm was 1/3.
N/N_C: ○: 0.70, ◎: 1.1
white alundum, J_S=0.030, d=2.5 cm, N/N_C=0.70

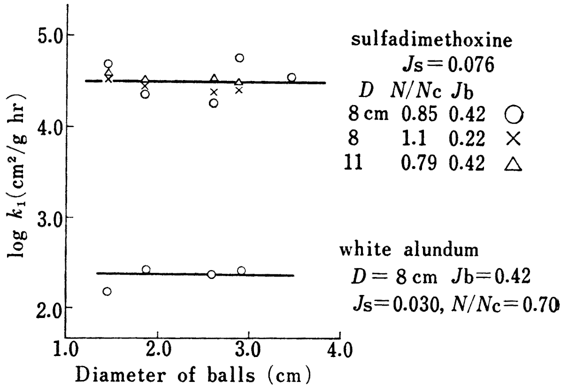

Fig. 9. Influence of the Diameter of the Balls on Parameter k_1 for Sulfadimethoxine and White Alundum (Ceramic mill)

5) Influence of the True Density of Balls on Parameters k_1 and k_2

The value of k_1 for ball-milling by stainless steel balls was larger than the value for ball-milling by ceramic balls. If k_1 was proportional to the γ th power of the true density of balls, γ was approximately 1.0 in case of N/N_c smaller than 1.0 and a little smaller than 1.0 in case of N/N_c larger than 1.0. (Table II). Parameter k_2 was influenced little by the true density of balls.

Table II. Influence of the True Density of Balls on Parameter k_1 for Sulfadimethoxine and White Alundum
Stainless steel mill: D=10cm, Ceramic mill: D=11cm J_S=0.076, J_b=0.42
The ratio of the number of balls in diameter of 2.5cm to that of balls in diameter of 1.9cm was 1/3.

	N/N_C	k_{1S}(cm²/g hr)	k_{1C}(cm²/g hr)	k_{1S}/k_{1C}	γ
Sulfadimethoxine	0.70	1.1×10^5	3.4×10^4	3.2	0.96
	1.1	1.2×10^5	4.2×10^4	2.9	0.87
White alundum	0.70	9.2×10^2	2.5×10^2	3.7	1.1
	1.1	7.0×10^2	2.8×10^2	2.5	0.75

k_{1s}: k_1 for ball-milling by stainless steel balls
k_{1c}: k_1 for ball-milling by ceramic balls

Tanaka reported that the rate of an increase of surface area by ball-milling was proportional to the product of P_c by P_σ, where P_c was the probability of collision between balls and powder particles and P_σ was the probability for powder particles to be broken after the collision with balls.[5] Parameter k_1 is represented by equation (5) or equation (5)′, when J_b is between 0.15 and 0.45, and N/N_c is constant.

5) T. Tanaka, *Ind. Eng. Chem. Process Design Develop.*, **5**, 353 (1966).

$$k_1 = KJ_b^{\alpha}J_s^{-\beta}\rho_b^{\gamma} \tag{5}$$

$$k_1 = K\{J_b^{(\alpha-\gamma)}J_s^{-(\beta-\gamma)}\}(\rho_b \cdot J_b/J_s)^{\gamma} \tag{5'}$$

K: A constant

The values of $(\alpha-\gamma)$, $(\beta-\gamma)$ and γ were tabullated in Table III. The energy given to a unit weight of powders in a unit time is considered to be related to the ratio of the total weight of balls to that of the sample, that is, to $\rho_b \cdot J_b/J_s$. Probably, $J_b^{(\alpha-\gamma)}J_s^{-(\beta-\gamma)}$ is related to P_c and $(\rho_b \cdot J_b/J_s)^{\gamma}$ is related to $P\sigma$ which is the probability concerned with crushing strength. The value of $(\beta-\gamma)$ for sulfadimethoxine is smaller than the value for white alundum. The powder particles of sulfadimethoxine are soft and sticky, while those of white alundum are hard and not so sticky as sulfadimethoxine particles. Physicochemical properties of powder particles, such as coherency between particles, may influence on $(\beta-\gamma)$.

TABLE III. The Values of $(\alpha-\gamma)$, $(\beta-\gamma)$ and γ for Sulfadimethoxine and White Alundum

	N/N_c	$(\alpha-\gamma)$	$(\beta-\gamma)$	γ
Sulfadimethoxine	0.70—0.85	0.8—1.1	0.4	1.0
	1.1	−0.9	0.3	0.9
White alundum	0.70	1.0	0.6	1.1
	1.1	−0.8	0.7	0.8